Eclipse PMR Holmium Laser System

Information for Use

Eclipse Surgical Technologies, Inc.
1049 Kiel Court
Sunnyvale, CA 94089
Main (408) 548-2100
FAX (408) 548-2168
Customer Service (800) 238-2205

Caution: Federal law restricts this device to sale by or on the order of a physician (or properly licensed practitioner). Federal law further restricts the use of this device to practitioners who have been trained in laser interventional cardiology including laser operation.

Caution: Use of this device is restricted to patients who have signed a procedure-specific consent form to ensure that the risks associated with PMR have been fully explained and understood.

1. DEVICE DESCRIPTION

The Eclipse PMR System is composed of the New Star Holmium: YAG Laser, the ECG monitor and delivery system catheters. The laser radiation emitted from this system has a wavelength of approximately 2.1 microns, which is in the mid-infrared (invisible) range of the electromagnetic spectrum. Water is the target absorber for this laser wavelength. This laser emits 350 microsecond laser radiation pulses at a 35 millisecond pulse repetition interval. The energy output from the laser aperture is 2.7 Joules while the clinical level is 2 Joules per pulse. The pulses are synchronized with the cardiac cycle through the ECG monitor which provides a trigger signal to allow synchronization of the heartbeat with the delivery of laser energy. There is a visible laser beam used for calibration.

The laser energy is delivered to the target tissue via an optical fiber. The Axcis PMR Delivery System has been designed for this purpose and consists of the Axcis Laser Catheter and the Axcis Aligning Catheter. The Laser Catheter contains a single solid core optical fiber of approximately 365 ?m diameter terminated with a quartz lens and contained within a braided PEBAX shaft. The Aligning Catheter is an approximately 9F braid-reinforced catheter which comes in 5 different tip configurations to facilitate access to various shaped cardiac anatomies.(see Section 10.3).

2. INDICATIONS FOR USAGE

The Eclipse PMR System is indicated for use in percutaneous myocardial revascularization (PMR) procedures to decrease angina and increase exercise tolerance in patients with chronic angina (Canadian Cardiovascular Society Class III or IV) which is refractory to medical treatment and secondary to objectively demonstrated coronary artery atherosclerosis and with a region of the myocardium with reversible ischemia not amenable to direct coronary revascularization.

3. CONTRAINDICATIONS

No contraindications known.

4. WARNINGS and PRECAUTIONS

See WARNINGS AND PRECAUTIONS in the final draft labeling (Information for Use).

- The Axcis PMR System may only be used with the New Star Laser.

Explosions or fire hazard - Do not operate the laser in the presence of flammable substances, including gases, anesthetics, cleaning agents, combustible materials, or other volatile substances. **Explosions or fire can result.**

- Combustible or flammable materials (for example drapes, gowns or gauze) may be ignited by laser radiation unless they are kept wet or moistened.
- Surround the procedure field with wet towels or wet gauze.
- Modify all other flammable materials to make them fire-retardant (for example flame resistant drapes and gowns). Minimize oxygen exposure as oxygen increases the combustibility of materials exposed to laser radiation.

Laser Radiation - The laser is classified as a Class IV laser product as defined in the Code of Federal Regulations (CRF 21 Section 1040.10(b)).

- Avoid exposure to laser radiation at all times during the installation and operation of the laser as direct or reflected radiation may damage skin or eyes.
- DO NOT LOOK DIRECTLY INTO THE Ho:YAG LASER BEAM as it can cause permanent ocular damage.
- Protect the patient's eyes by covering them with wet gauze or protective eyewear.
- All catheterization laboratory personnel must wear protective eyewear with a minimum optical density of 3 at a wavelength of 2.1 ?m when the laser is in use.

Physician Training

- The Eclipse PMR System should only be used by properly trained cardiologists (see Section 11.3 Operator Training).

Handling and Sterilization of the Axcis PMR Delivery System

- The Axcis Laser Catheter and Axcis Aligning Catheter are sterilized with EtO gas and are **for single use only**. **Do not re-sterilize or reuse**.
  - Inspect sealed sterile package before opening. Product is sterile only in unopened, undamaged package. If package is opened or damaged, or if seal is broken, contents may not be sterile and may cause infection in the patient.
  - Do not bend the fiberoptic at sharp angles. The Axcis Laser Catheter should not be bent beyond a bend radius of 7 mm.
  - The Introducer Tool is reusable and can be cleaned and re-sterilized.
    - Pre-cleaning (Introducer Tool only): Rinse the tool thoroughly using lukewarm water (below 43?C/110?F).
    - Cleaning (Introducer Tool only): Clean using a low-sudsing, protein-dissolving detergent or a combination of an enzymatic cleaner followed by a manual detergent. Follow manufacturer's instructions regarding concentration, temperature, contact time and reuse. Clean using a soft-bristle brush. Do not soak in hot water, alcohol, disinfectants or antiseptics to avoid coagulation of blood or other body fluids. Do not use steel wool, wire brushes or abrasive detergents.
    - Rinse thoroughly with water to remove all traces of debris or cleansing agents. **Inspect the Introducer Tool to ensure that it is undamaged and that the slot width is uniform.**
    - Sterilization (Introducer Tool only): The Introducer Tool should be sterilized in a gravity-displacement steam-sterilization cycle of 15 minutes at a minimum of 132?C (270?F) or a pre-vacuum steam-sterilization cycle of 4 minutes at a minimum of 132?C (270?F).
  - **Biohazard** -- After use, handle and dispose of the Laser and Aligning Catheters as appropriate for a biohazard.

Precautions During PMR

- The wall thickness in the targeted region should be assessed by echocardiography prior to the PMR procedure. PMR should not be performed in areas of the myocardium that are:
  - less than 8 mm in wall thickness
  - infarcted
  - in the region of the mitral valve or mitral valve apparatus
  - in the region of the papillary muscle
  - in the region of a left ventricular mural thrombus
- PMR should only be performed under fluoroscopic observation and care must be taken not to duplicate channel locations. Firing the laser into a previously formed channel may cause perforation.
- The Axcis PMR Delivery System consists of devices that are delicate and must be manipulated carefully.

- The Axcis PMR Delivery System is stiffer than standard PTCA guiding catheters and can potentially place significant force on the heart wall. Care must be taken not to bend or wedge the optical fiber by pushing the lens too vigorously against the myocardium.
- Do not fire the laser when the lens is retracted within the Aligning Catheter. Always retract the lens before repositioning the Laser Catheter.
- If the Axcis PMR Delivery System does not move freely, the catheters may be wedged within the left ventricle or the lens may be entrapped within trabeculae or the cordae tendinae. In this case, the Laser Catheter and lens should be withdrawn into the Aligning Catheter. The Aligning Catheter should then be withdrawn into a position that frees the device.
- The proximal end of the Laser Catheter should not be rotated more than two revolutions in instances in which the distal end is not rotating. Further rotation may result in kinking or other mechanical failure of the catheter.
- The Aligning Catheter may be used for manual contrast injections using a syringe only. The Aligning Catheter should not be used with a power injector. The Laser Catheter should not be used for contrast injection.
- If the patient experiences ventricular fibrillation during the procedure, discontinue the procedure and treat the arrhythmia as appropriate. A defibrillator should be readily available at all times during the procedure.

5. ADVERSE EVENTS

5.1 Observed Adverse Events

The randomized trial of PMR, the PACIFIC Study, used the Eclipse PMR System to compare treatment plus maximal anti-anginal medications (PMR+MEDs) with medical management alone (MEDs). The study enrolled 200 patients who were followed for an average of 11.1 months.

There were no intra-procedural deaths in the study. Within 30 days of treatment, one PMR+MEDs patient died of cardiac causes. During 12 months follow-up, an additional 6 PMR+MEDs patients died (5 from cardiac causes and 1 from respiratory arrest) and 2 subjects in the MEDs group died (both due to cardiac causes).

Serious Averse Events which occurred in the study are summarized in **Table 1**.

Table 1. Serious Adverse Events

Includes all adverse events, both related and unrelated to PMR, sorted by system affected.

	PMR+MEDs (n=100)		MEDs (n=100)	
Event[1]	**Patients with Event**	**Number of Events**	**Patients with Event**	**Number of Events**
All CV events combined	50	108	48	103
Angina	25	49	39	74
Arrhythmias[2]	11	12	4	6
Death (all causes)	7	7	2	2
Heart Failure	8	8	2	2
Injury to heart structure (perforation)	3	3	0	0
Myocardial infarction	11	12	5	8
Other cardiovascular[3]	16	18	7	9
Thromboembolic disorder	4	4	2	3
All DER Events Combined	1	1	2	3
All GU Events Combined	2	2	2	2
All GEN Events Combined	10	11	7	7
All GI Events Combined	8	12	3	4
All NEU Events Combined	3	4	1	1
All PSY Events Combined	2	2	1	2
All RES Events Combined	7	10	3	4
All AE Combined	56	159	52	130

[1]Abbreviations: CV = cardiovascular, DER = dermatologic, GEN = general, GI = gastrointestinal, GU = genitourinary, HEM = hematologic, LAB = laboratory, MET = metabolic, MUS = musculoskeletal, NEU = neurologic, PSY = psychiatric, RES = respiratory, AE = adverse events.

[2]Arrhythmias (number of patients with each in treatment/control groups) were: arrhythmia (0/2), ventricular arrhythmia (1/0), AV block complete (1/0), bradycardia (4/1), atrial fibrillation (2/0), atrial flutter (2/0), heart block (1/0), tachycardia (0/1).

[3]Other cardiovascular events (number of patients with each in treatment/control groups) were: heart arrest (4/0), syncope (2/2), vascular disease peripheral (3/2), amblyopia (0/1), vascular anomaly (1/0), cellulitis (1/0), creatine PK increase (1/0), pericardial effusion (1/0), embolism (1/0), hypotension (1/0), artery occlusion (0/1), carotid occlusion (0/1), coronary stenosis (1/0), ulcer (1/0).

5.2 Potential Adverse Events

Adverse events potentially associated with the use of PMR, but not observed in the study, include (in alphabetical order):

- Allergic reaction to contrast agent
- Arterial Dissection
- Bleeding
- Cardiogenic shock
- Fragmented catheters and lens tip
- Left ventricular dysfunction
- Renal insufficiency
- Vascular damage

6. CLINICAL STUDIES

Purpose: The purpose of the PACIFIC Study was to compare PMR plus medication (PMR+MEDs) with medication alone (MEDs). Primary outcome measures were angina improvement and improvement in exercise tolerance testing. The secondary outcome measure was improvement in quality of life.

Design and Patients: This multi-center, prospective, randomized controlled trial was conducted at 11 U.S. centers. The study was conducted between November 1997 and August 1999 with 200 patients enrolled, 100 randomized to PMR+MEDs and 100 randomized to MEDs. There were 17 withdrawals from the study and 9 deaths. All of the remaining 174 patients reached one year follow-up. Baseline characteristics and cardiac risk factors were similar between the two groups.

Methods: PMR was performed using a percutaneous access route typical of other interventional cardiac procedures. The Laser Catheter containing the fiberoptic was introduced through the Aligning Catheter and used to apply laser energy to the endocardial surface of the left ventricle. As the fiber was advanced, pulsed laser energy was delivered to the myocardium until the optical fiber tip penetrated to a depth of 8 mm or less. PMR channels were placed approximately 1 cm apart using fluoroscopic visualization for catheter placement. The laser was synchronized to fire at the electrocardiographic R-wave, when the left ventricle was at maximum contractile width.

Results: The number of PMR channels created during the procedure ranged from 8 to 35 (mean 16.1), using an energy of 2 Joules per pulse. **Table 2** summarizes the principal safety and effectiveness results. Patients treated with PMR experienced statistically significant improvements in angina, exercise tolerance test duration and quality of life. There was no significant difference in mortality or serious adverse events between the groups. The ejection fraction and wall motion scores at 3 months were not significantly different than at baseline, demonstrating that the PMR procedure did not adversely affect left ventricular function.

Table 2. Principal Safety and Effectiveness Results

All patients in the Randomized Trial (n=200)	PMR+MEDs (n=100)	MEDs (n=100)	P-value
Angina Improvement			
Success	42.0% (n=42)	8.0% (n=8)	<0.001
Failure	58.0% (n=58)	92.0% (n=92)	
12-Month Angina Distribution			
None	0.0% (n=0)	1.0% (n=1)	0.001
Class I	29.0% (n=29)	4.0% (n=4)	
Class II	35.0% (n=35)	11.0% (n=11)	
Class III	14.0% (n=14)	44.0% (n=44)	
Class IV	15.0% (n=15)	38.0% (n=38)	
Mortality	7.0% (n=7)	2.0% (n=2)	0.170
Exercise Tolerance Improvement (seconds)	50.8 (n=99)	-6.4 (n=97)	0.014
Quality of Life Improvement (SAQ)			
Physical Limitation Scale	12.3 (n=95)	10.4(n=95)	<0.001
Anginal Stability Scale	26.0 (n=96)	4.2 (n=96)	<0.001
Anginal Frequency Scale	19.3 (n=95)	7.1 (n=97)	<0.003
Treatment Satisfaction Score	9.4 (n=96)	1.7 (n=97)	<0.001
Disease Perception Score	28.5 (n=96)	9.1 (n=97)	<0.001

Angina Improvement: Success was defined as improvement of 2 or more CCSAS classes from baseline to 12 months.
12-Month Angina Distribution: Distribution of angina at 12 months by CCSAS class as assessed by the Clinical Investigator at each site.
Mortality: Proportionate analysis p = 0.170 by 2-Tail Fisher's Exact Test and 0.089 by Kaplan Meier Analysis, Log Rank Test.
Exercise Tolerance Improvement: Improvement in exercise duration in seconds from baseline to 12 months.
Quality of Life Improvement: Seattle Angina Questionnaire analysis scores improvement from baseline to 12 months. Higher scores indicate higher quality of life.

There were no intra-procedural deaths in the PACIFIC Study. Within 30 days of treatment, one PMR+MEDs patient died of cardiac causes. During 12 months follow-up an additional 6 PMR+MEDs patients died (5 from cardiac causes and 1 from respiratory arrest) and 2 subjects in the MEDs group died (both due to cardiac causes).

The results of the PACIFIC Study are supported by the results of the BELIEF Study, a double blinded comparison between PMR+MEDS and Sham treatment (Sham+MEDs). In the BELIEF Study 41% (16/39) of the PMR treated patients experienced $\geq$ 2 class improvement in angina compared with 13% (5/39) of the Sham treated patients. There was one intra-procedural death in the Sham+MEDs group and another at 3 months (5%; 2/42). There were no deaths in the PMR treated group (0/40; p=0.49). There was one myocardial perforation requiring pericardiocentesis in the PMR+MEDs group and one instance of pericardial effusion at 3 months follow-up in the Sham group. There were 2 episodes of TIA in the Sham group and none in the PMR group and there were no MI in either group. Other adverse events included extra systole ventricular arrhythmias, groin complications, need for analgesics, and

hospitalizations. There was no significant difference between the two groups for any of the adverse events.

7. PATIENT SELECTION AND TREATMENT

Specific Patient Populations

The safety and effectiveness of the Eclipse PMR System has not been established for the following specific populations:

- patients under the age of 18;
- patients who are pregnant, undergoing labor and delivery or are nursing mothers;
- patients suffering from active hepatic disease, renal failure, cancer or major infection;
- patients with a left ventricular ejection fraction less than 30%;
- patients with CCSAS class II or better or;
- patients with myocardial ischemia limited to the right ventricular wall.

8. PATIENT COUNSELING INFORMATION

This device is restricted to use in patients who sign a procedure-specific informed consent to ensure that the risks associated with PMR have been fully explained to, and understood by, the patient.

Patients should be advised that any reduction of angina may occur gradually, that they should continue their anti-anginal medications, and that the need for these medications will be re-evaluated at subsequent visits.

Patients should be advised of the risks of the procedure including the possibility of:

- recurrence of angina;
- progression of myocardial ischemia;
- worsening heart failure;
- cardiac arrhythmia
- perforation and;
- death.

9. CONFORMANCE TO STANDARDS

The New Star Laser has been tested to and conforms with the requirements of the following domestic and international standards:

- IEC601-1:1988 Medical Electrical Equipment, General Requirements for Safety
- IEC60601-1-2:1993 Medical Electrical Equipment, General Requirements for Safety, Collateral: Electromagnetic
- IEC601-2-22:1992 Medical Electrical Equipment, Particular Requirements for the Safety of Diagnostic and Therapeutic Laser Equipment.
- 21CFR Part 1040.10 Laser Product Performance Standard

- EN55011:1998 Class A, the European Electromagnetic Emissions Standard
- IEC 825-1 Radiation Safety of Laser Products & Equipment

The ECG monitor meets the requirements of:

- EN55011, Group I, Class A 1991 Conducted Emissions and Radiated Emissions
- EN 61000-4-2, 1995-01 Electrostatic Discharge Immunity
- EN 61000-4-3, 1995-02 Electromagnetic Immunity
- EN 61000-4-4, 1995-01 Electrical Fast Transient/Burst Immunity
- En 50141 1994 Conducted Disturbance Induced by RF Fields

10. HOW SUPPLIED

10.1 Packaging

The Eclipse PMR System consists of the New Star Laser, the ECG monitor, the disposable Axcis PMR Delivery System (Axcis Laser Catheter, and Axcis Aligning Catheter) and the Introducer Tool.

- The New Star Laser and ECG monitor are initially installed in the hospital by Eclipse personnel.
- The single-use delivery systems are supplied sterile for every PMR case. Sterility may be compromised if the package is opened or damaged. Do not re-sterilize the Axcis Laser or Aligning Catheters.
- The Introducer Tool may be re-used if desired and must be cleaned and sterilized according to the appropriate procedures (see Section 4).

10.2 Storage

All delivery system catheters should be stored under conditions that protect against extremes of temperature and humidity. Products should be stored in a clean, dry environment, protected from water. Do not stack other objects on packaging to avoid crushing. Proper stock rotation should be practiced. Store in a cool, dry area. Do not expose to organic solvents, ionizing radiation or ultraviolet light.

10.3 Axcis PMR Delivery Systems

Axcis Laser Catheter	fiberoptic which delivers laser energy
Axcis Aligning Catheter	Ultra-1, Ultra-1 Long Ultra-2, Ultra-3, and Open-2 configurations to reach various cardiac anatomies
Introducer Tool	tool used to insert the Laser Catheter into the Aligning Catheter
SMA Cleaning Kit	lint-free swabs and pre-moistened pads to clean the connector on the Laser Catheter

11. CLINICIAN USE INFORMATION

11.1 Patient Informed Consent

A PMR procedure-specific consent form must be signed by each patient to ensure that the risks associated with PMR have been fully explained to the patient.

11.2 Device Operating Instructions

Operating instructions for the laser and ECG monitor are contained in the Eclipse PMR Holmium Laser User Manual which includes sections describing the system specifications, operation of the laser, laser safety, labeling, troubleshooting and calibration and ECG monitor operation. It also contains a glossary of laser terms.

It is essential that the User Manual, especially those parts dealing with laser safety, be read and understood before operating, maintaining, or servicing this system. Failure to operate the New Star Laser in accordance with the User Manual may result in serious injury.

Specific instructions for use are provided with each Axcis PMR Delivery System device and these should be read in conjunction with this Information For Use document.

11.3 Operator Training

Federal law restricts the use of this device to practitioners who have been trained in percutaneous myocardial revascularization including laser system operation. Operator training for use of the Eclipse PMR System must include training in the use of the laser system and the fiberoptic delivery systems, as well as appropriate clinical training.

Laser Training:

The American National Standards Institute offers the following Standard of Practice for the Use of Lasers in Medicine and Surgery**:**

ANSI Z136.3, "American National Standard for Safe Use of Lasers in Health Care Facilities," 1996.

Clinical Training:

Use of the Eclipse PMR System should only be undertaken by personnel who have met the standards of the Eclipse continuing education training program, which includes didactic and hands-on training covering:

- patient selection
- PMR procedures
- laser safety and operation

Further information about training can be obtained from an Eclipse Surgical Technologies, Inc. representative at 800-741-7062.

11.4 Mechanism of Action

The mechanism(s) whereby myocardial revascularization relieves angina is not known. Current theories include:

- Increased collateralization via angiogenesis;
- Symptom reduction resulting from disruption of pain fiber function;
- Increased perfusion of myocardium by the channels created
- Placebo effect

12. PATIENT'S MANUAL

The brochure "Information for Patients Considering Percutaneous Myocardial Revascularization" provides general information to the potential patient regarding the risks and benefits associated with the PMR treatment.